REMARKS

This Amendment and Response is filed in response to the Office Action dated February 7, 2003. Initially, Applicant's attorney wishes to thank the Examiner for the careful attention given the present application. In addition, Applicant's attorney is appreciative of the courteous interview extended by both Examiner Nichols and Examiner Spector on April 3, 2003 in the instant application. Although formal agreement was not reached during the interview, a general consensus and substantial progress in this regard was made. The issues discussed in the interview are reflected in the amendments to the claims presented herein and the remarks presented below.

Claims 1-7 are under examination and claims 8-20 are withdrawn from consideration as discussed above. Claims 1-7 are pending in this application and claims 8-20 have been cancelled from current consideration without prejudice to presentation in this or a later filed application. Additionally, new claims 22-43 have been introduced to reflect the language discussed during the interview.

Initially, the drawings have been objected to because of margin issues. A new set of figures with proper margins is submitted herewith for the Examiner's review and consideration. Additionally, the abstract of the disclosure has been objected to because it is too long. An abstract of less than 150 words is provided herein by amendment. Accordingly, these objections should be withdrawn.

Claims 1-6 stand rejected under 35 U.S.C. 102(b) as being anticipated by Westaby et al., "Serum S100 Protein: A Potential Marker for Cerebral Events During Cardiopulmonary Bypass" Ann. Thorac. Surg. 61: 88-92 (1996) ("Westaby"); and Claim 7 stands rejected under 35 U.S.C. 103(a) as being obvious over Westaby in view of Herrmann et al., "Release of Glial Tissue-Specific Proteins After Acute Stroke" (2000) ("Hermann") and Strachan et al. Measurements of serum NSE and S100 concentrations (2000) ("Strachan").

As was discussed during the interview, a number of important features exist in the present application that distinguish it from the prior art. Importantly, the present invention uncouples the prior art's link between S100β and neuronal damage. In other words, detection of S100β in the blood stream does not necessarily mean that brain damage has occurred, but rather that the blood brain barrier ("BBB") has opened and released S100β into the blood. As was discussed and agreed during the interview, each of the teachings in the prior art, couple S100β

detection with neuronal damage. The present claims highlight a number of distinctions from the art. Specifically, there are: (i) temporal distinctions between BBB permeability and brain damage (either as a result or cause of BBB opening); (ii) distinctions between the type of subjects who are in need of such detection techniques; and (iii) distinctions in that the present invention correlates differing levels of S100β in the blood to indicate a subject's state of health. Each of these distinctions are patentable embodiments of the present invention.

(I) Temporal Issues

Independent claim 1 has been amended to recite that the levels of S100β in a blood sample derive from the subject are detected prior to manifestation of neuronal damage in the subject. Claims 7 and 21 have been presented in this series to reflect the fact that when statistically relevant levels of S100β are detected in the blood stream that the method also includes monitoring the level of other markers of neuronal distress such as NSE, GFAP and a second level of S100β protein release into the blood stream. These claims now reflect the temporal distinction discussed during the interview. As was discussed and agreed these amendments distinguish over the prior art. Accordingly, it is respectfully submitted that these claims are in condition for final allowance and notice to such effect is respectfully requested.

(II) Type of Subject Aspects

Claims 21-37 have been added to reflect the particular type of subject to which the present application has particular suitability. As reflected in independent claim 21, the present invention is useful for a subject that is free of neuronal damage, or as is reflected in claims 27, wherein the subject is predisposed to brain damage but is free of symptoms of brain damage at the time of the diagnosis. As was discussed and agreed upon, this important distinction in subjects is reflective of the novel and non-obvious features of the present invention. Specifically, a person who is free of neuronal damage may have blood brain barrier permeability (e.g. after extended exercise there is "leakage" of the BBB), however, opening of the BBB is an important factor in determining how to diagnose, treat or care for a patient or subject. None of the prior art appreciates this aspect of the present invention and it is asserted that claims 21-37 are in condition for allowance and it is respectfully submitted that they be passed to issue.

(III) Varying Levels of S100β

Finally, claims 38-43 have been amended to reflect the fact that one embodiment of the present invention is to detect varying levels of S100β released into the blood stream and correlate that with permeability of the BBB without neuronal damage and permeability of the BBB with neuronal damage. As discussed during the interview, no prior art anticipates nor makes obvious such a stepwise detection of S100β in the blood stream to detect first opening of the blood brain barrier and then onset of neuronal damage. It is respectfully submitted that these claims are in condition for allowance and notice to such effect is respectfully requested.

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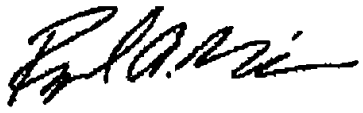
AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for this Amendment, or credit any overpayment, to deposit account no. 50-0436.

Respectfully submitted,

PEPPER HAMILTON LLP



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